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TITLE: Substituted imidazolidine derivatives, their preparation, their use and pharmaceutical preparations including them

Brief Summary Text (6):

The integrins are a group of adhesion receptors which play an important part in cell-cell-binding and cell-extracellular matrix-binding processes. They have an .alpha..beta.-heterodimeric structure and exhibit a wide cellular distribution and a high extent of evolutive conservation. The integrins include, for example, the fibrinogen receptor on platelets, which interacts especially with the RGD sequence of fibrinogen, or the vitronectin receptor on osteoclasts, which interacts especially with the RGD sequence of vitronectin or of osteopontin. The integrins are divided into three major groups, the .beta.2 subfamily with the representatives LFA-1, Mac-1 and p 150/95, which are responsible in particular for cell-cell interactions of the immune system, and the subfamilies .beta.1 and .beta.3, whose representatives mainly mediate cell adhesion to components of the extracellular matrix (Ruoslahti, Annu. Rev. Biochem. 1988, 57, 375). The integrins of the .beta.1 subfamily, also called VLA proteins (very late (activation) antigen), include at least six receptors which interact specifically with fibronectin, collagen and/or laminin as ligands. Within the VLA family, the integrin VLA-4 (.alpha.4.beta.1) is atypical, insofar as it is mainly restricted to lymphoid and myeloid cells and is responsible in these for cell-cell interactions with a large number of other cells. For example, VLA-4 mediates the interaction of T and B lymphocytes with the heparin II-binding fragment of human plasma fibronectin (FN). The binding of VLA-4 with the heparin II-binding fragment of plasma fibronectin is especially based on an interaction with an LDVP sequence. In contrast to the fibrinogen or vitronectin receptor, VLA-4 is not a typical RGD-binding integrin (Kilger and Holzmann, J. Mol. Meth. 1995, 73, 347).